Reviewer's report

Title: Sequence variation in telomerase reverse transcriptase (TERT) as a determinant of risk of cardiovascular disease: the Atherosclerosis Risk in Communities (ARIC) Study

Version: Date: 9 November 2014

Reviewer: Matthew D'Mello

Reviewer's report:

Major Changes:

Background
It is unclear why only TERT was focused on and not TERC? Both the reverse transcriptase and the RNA component are required to extend telomeres. RS10936599 (TERC gene) was the strongest association reported in the Codd et al. 2013 paper. Please address why this was specifically selected.

Methods
A power calculation would be useful. Effect sizes are expected to be minute and perhaps the study was not powered enough to detect some associations.

Discussion
The discordant findings between the Women’s Genome Health Study (WGHS) reported by Zee et al., (2011) and the present ARIC study warrant further explicit discussion. ARIC had many more events and a longer follow-up period, yet associations that were significant in WGHS were non-significant in ARIC.

Minor Changes:

General
Report confidence intervals with hazard ratio

Abstract
Line 54: How is the variant associated with mean telomere length? Is it associated with increased/decreased length?

Methods
Line 144: Should read “Six SNPs” rather than “Six (6) SNPs”
State whether the assumptions of the cox proportional hazard models were met.
Specify in manuscript text, report the variables adjusted for in the cox proportional hazard models.
Specify in manuscript text, the statistical tests used to generate p-values in the provided tables.
Results
Tables- 4,5,6 – please indicate the number of events in each ethnic group within the table

Discussion
A further limitation is the lack of a replication cohort. As the reported p-values are quite modest, replicating these findings with another population would strengthen the reported results.

Discretionary Revisions:
Background
A brief comment regarding the bi-racial make-up of the ARIC study would be beneficial.
Relatively few studies have looked at telomerase variants in an African-American population and it is indeed a unique aspect of the report.

Level of interest:An article whose findings are important to those with closely related research interests

Quality of written English:Acceptable

Statistical review:Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests